Proposal to national Health Technology Assessments (Norway)

Proposals to national Health Technology Assessments (HTA) will be published in its entirety. Please contact the Secretariat before submission if necessary information for completing the form cannot be published.

The proposer know that this form will be published in its entirety: ☒

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1. Title of proposal:

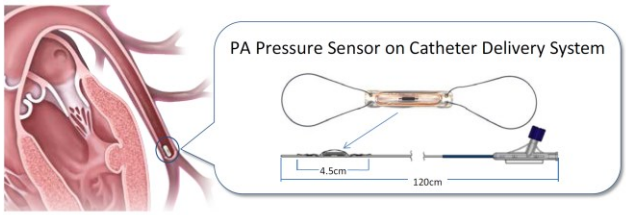
Continuous monitoring of pulmonary artery pressure via an implanted leadless and battery less pressure sensor for the management of patients with moderate to severe heart failure (New York Heart Association class III)

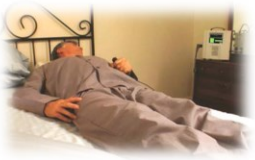
2. Brief description of the technology:

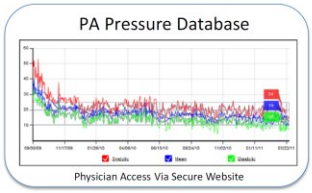
The device can be implanted in the pulmonary artery of NYHA class III heart failure patients during a minimally invasive catheter based procedure. The sensor is implanted via a catheter introduced into the right femoral vein and advanced through the venous system into the pulmonary artery. The procedure is similar to a right heart catheterisation procedure (common in heart failure patients) and has a low complication rate and similar low risk profile to right heart catheterisation.

The system consists of three components: the implantable device; the home monitoring unit and a secure database storing the recorded pressure data accessible by the physician responsible for that patients care.

Patients record their pulmonary artery pressures once a day using the home monitoring unit which transmits this pressure recording to the database where it can be regularly reviewed by their physician. Weekly review of the pressure recordings by physicians is sufficient for the technology to be effective.







3. Brief description of current situation (Which technology (s) is currently in use? Status for technology (providing curative treatment, extended life etc.) Will the technology proposed assessed replace, or be in addition to current situation?)

There are currently no alternative systems providing continuous pulmonary artery pressure monitoring. There are systems which report daily patient body weights in an effort to predict episodes of acute heart failure but these systems have not demonstrated the same efficacy as internal pressure monitoring.

4. The technology applies?

New technology ☒ ☐

A new recommended use or a new indication for an established technology	☐	☐
A comparison of several technologies	☐	☐
An existing technology already in use	☐	☐
If yes - used in clinical practice?	☐	☐
If yes - adopted in research / testing?	☐	☐

Physicians can use the pulmonary artery pressure recordings to assist in managing the patient's medication. Physicians should prescribe treatment to keep patients pressures within an optimal therapeutic range.

The pulmonary artery pressure rises in the days preceding episodes of acute heart failure. These events are life threatening if not treated quickly, treatment requires emergency admission to hospital, intensive monitoring and medical therapy in the first few days of the admission and a lengthy stay to stabilise patients. Currently patient symptoms are the only guide to impending hospitalisation and when symptoms manifest it is too late to avoid the hospitalisation.

The pulmonary artery data can give an early warning of episodes of acute heart failure and allow physicians to make changes to those patients drug therapy in order to stabilise them before the event requires hospitalisation and before the event becomes life threatening.

5. The technology involves (several options are possible)**?**

Pharmaceuticals	☐
Medical devices	☒
Procedures	☐
Screening	☐
Highly specialized services /national services	☐
Organisational structure of health services	☐
Other (Please describe)	☐

6. The technology's utility area:

Preventive health care	☐
Assessment and diagnosis	☒
Medical treatment	☒
Rehabilitation	☐
Specialist health services	☐
Primary health services	☐

The technology provides diagnostic data to guide heart failure treatment. In contrast to other diagnostic technologies the implantable pulmonary artery pressure provides continuous diagnostic data for the lifetime of the patient, there is no battery. Therefore the treatment effect can be considered as a lifetime benefit.

7. Does the technology involve use of radiation (ionizing / non ionizing) ☐

Please shortly describe type of radiation, equipment and exposure

8. Which clinical disciplines are involved by the technology, and which patient groups are affected? (Are other groups affected by the technology (personnel, relatives)?

The sensor should be implanted by physicians skilled in catheter based cardiac procedures.

Sensors should be implanted in NYHA III heart failure patients with a history of heart failure hospitalisations as recommended by a specialised heart failure physician.

Hospitals that are specialised in treating heart failure should decide how to integrate the pressure monitoring component into their existing heart failure management program. Some centres may want to divide the responsibility of regularly reviewing patient pressure data among a team of specialists, which could include specialist nurses as well as or instead of physicians whilst other physicians might prefer to do this task themselves.

The choice of action based on changes in pulmonary pressure data should be made by the heart failure specialist physician responsible for that patient's treatment.

9. Which aspects are relevant for the assessment? (several options are possible)

Clinical effectiveness	☒
Safety/adverse effect	☒
Costs/use of resources	☒
Cost efficiency	☒
Organisational consequences	☒
Ethical	☐
Legal	☐

10. **Please identify the main research question, as well as any sub questions** (in accordance with section 8):

Category	**Criteria**
Population	Patients with a diagnosis of moderate to severe HF (NYHA class III) for 3 months, on a stable and optimised medication regimen, and have had a HF-related hospitalisation within the previous 12 months
Intervention	CardioMEMS™ HF System, in addition to usual practice
Comparator	Usual practice
Outcomes to be assessed	HF-related hospitalisations; QALYs; Mortality; Safety (device-related and procedure-related)
Healthcare resources to be considered	Hospital stay Medical staff Nursing staff Medications Surgical devices and consumables

11. Please shortly describe why it is important to perform an HTA on the proposed technology

The CardioMEMS system has randomised clinical evidence demonstrating its safety and efficacy in reducing heart failure hospitalisations in NYHA III heart failure patients with a history of heart failure hospitalisations.

This is a new telemonitoring diagnostic technology available to patients in the US following FDA approval which although CE marked for use in Europe has not been evaluated within the context of European healthcare systems or by any HTA agencies.

An HTA performed by a European HTA agency is now the next step in making this technology available to European heart failure patients.

12. Please comment on the proposed technology in relation to:

Severity

Heart failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The ESC definition of heart failure is “an abnormality of cardiac structure or function leading to a failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at the expense of increased filling pressures)[1]. Clinical definitions vary but the ESC suggest the following and use this in the latest update of their heart failure guidelines “a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function”[2]. Diagnosis can be difficult and if a diagnosis is suspected based on clinical grounds (medical history, clinical signs and symptoms) then this should be supported and confirmed by objective evidence of cardiac dysfunction.

The main causes of heart failure are structural abnormalities resulting from ischemic heart disease, although there are many other conditions which can lead to heart failure such as hypertension, cardiomyopathies, valvular and congenital heart disease, myocarditis, pulmonary hypertension and cardio-toxic substances.

The cardinal manifestations of HF are dyspnoea and fatigue, which may limit exercise tolerance; and fluid retention, which may lead to pulmonary oedema and/or peripheral oedema. There are two distinct heart failure aetiologies heart failure with reduced ejection fraction (HF-REF, also called systolic heart failure) and heart failure with preserved ejection fraction (HF-PEF, also called diastolic heart failure. Treatment for both types is predominantly pharmacological although there is no convincing evidence to support any treatment for HF-PEF[2]. HF-REF patients with a broad ECG QRS complex (>120ms) and remaining in New York Heart Association (NYHA) class II to III despite drug therapy are indicated for implantation with cardiac resynchronisation devices and patients with narrow QRS with ICD’s[2]

HF is a progressive disease associated with high patient morbidity and mortality and a poor quality of life. Prognosis following a diagnosis of heart failure is poor and 5 year survival rates compare badly with those of most cancers[5], heart failure is incurable and whilst patients may die from other causes not directly linked to heart failure once diagnosed with heart failure they will not be cured of the syndrome by any currently available therapy.

Patients with a heart failure diagnosis are generally referred to as suffering chronic heart failure and will be managed out of hospital in many cases by general practitioners. If onset or change in heart failure signs and symptoms is sudden then patients are considered to be suffering Acute Heart Failure (AHF). AHF is a life threatening condition usually resulting in urgent hospitalisation. Onset of AHF can vary from very sudden (perhaps triggered by ventricular arrhythmia or acute myocardial infarction “MI”) to deterioration over a period of days or weeks, characterised by increasing dyspnoea or oedema[2]. AHF is treated pharmacologically, in general the aim is to stabilise patients using combinations of oxygen, diuretics and vasodilators. Opiates and inotropes are sometimes used and rarely mechanical circulatory support, non-invasive and occasionally invasive ventilation.

A recently published study based on data from patients covered by the national health insurance general scheme in France highlights the burden that heart failure hospitalisations place on hospitals[7]. The study included 69,958 incident hospitalisations for heart failure. Mean length of stay for each hospitalisation was 9 days. Patients hospitalised for the first time with heart failure accounted for 1.2% of all patients hospitalised in France in 2009; 2.6% of all hospitalisations for patients aged 70-79 years; 6.2% for those aged 80-89 years and 10.9% of patients hospitalised aged 90 years and above. The mortality rate for these first hospitalisations was 6.4% and 4.4% during 30 days after discharge with no readmission for 75% of those deaths. In patients who survived 30 days after discharge 18% were readmitted at least once.[7]

Expected effect of treatment

One previous randomised controlled trial, CHAMPION, has been conducted in the United States[3].

The primary efficacy endpoint of the CHAMPION trial was the rate of hospitalizations for heart failure (as adjudicated by an independent blinded Clinical Events Committee) during the first 6 months of Randomized Access. There were 84 heart failure hospitalizations in the Treatment group compared with 120 heart failure hospitalizations in the Control group. This difference between the groups represented a 28% reduction in the rate of hospitalization for heart failure in the Treatment group (0.32 hospitalizations per patient in the Treatment group vs. 0.44 hospitalizations per patient in the Control group, p = 0.0002), (Table 1).

	Number of Heart Failure Hospitalizations	**6 Month Rates of Hospitalization for Heart Failure**	**Hazard Ratio (95% CI) [p-value]**
Treatment Group (n=270)	84	0.32	0.72 (0.60-0.85) p=0.0002
Control Group (n=280)	120	0.44	

Table 1: Primary Efficacy Endpoint- Rates of Hospitalization for Heart Failure during First 6 months of Randomized Access

Safety

The study met the two primary safety endpoints: (1) freedom from device/system related complications (DSRC) and (2) freedom from sensor failure. The protocol pre-specified objective performance criterion (OPC) were that at least 80% of patients were to be free from DSRC and at least 90% were to be free from pressure sensor failure. Of the 575 patients in the safety population, 567 (98.6%) were free from DSRC at 6 months (lower confidence limit 97.3%, p<0.0001) (Table 2). This lower limit of 97.3% is greater than the pre-specified OPC of 80%. There were no sensor explants or repeat implants and all sensors were operational at 6 months for a freedom from sensor failure of 100% (lower confidence limit 99.3%, p<0.0001) (Table 3). This lower limit of 99.3% is greater than the pre-specified OPC of 90%.

Device/System Related Complications (n=575)		**Lower 95.2% Confidence Limit[2]**	**Objective Performance Criterion (OPC)**	**p-value[3]**
Yes	**No**			
8 (1.4%)[1]	567 (98.6%)	97.3%	80%	p<0.0001

[1] DSRCs (8 total) by group: Consented but not randomized (2), Treatment (3), Control (3)

[2] Exact 95.2% Clopper-Pearson lower confidence limit

[3] p-value from exact test of binomial proportions compared to 80% for all patients

Table 2: Primary Safety Endpoint – Freedom from Device/System Related Complications

Pressure Sensor Failures (n=550)		**Lower 95.2% Confidence Limit[2]**	**Objective Performance Criterion (OPC)**	**p-value[3]**
Yes	**No**			
0 (0.0%)	550 (100%)[1]	99.3%	90%	p<0.0001

[1] Pressure sensor failure counts by group: Treatment (0), Control (0)

[2] Exact 95.2% Clopper-Pearson lower confidence limit

[3] p-value from exact test of binomial proportions compared to 90% for all patients

Table 3: Primary Safety Endpoint – Freedom from Pressure Sensor Failures

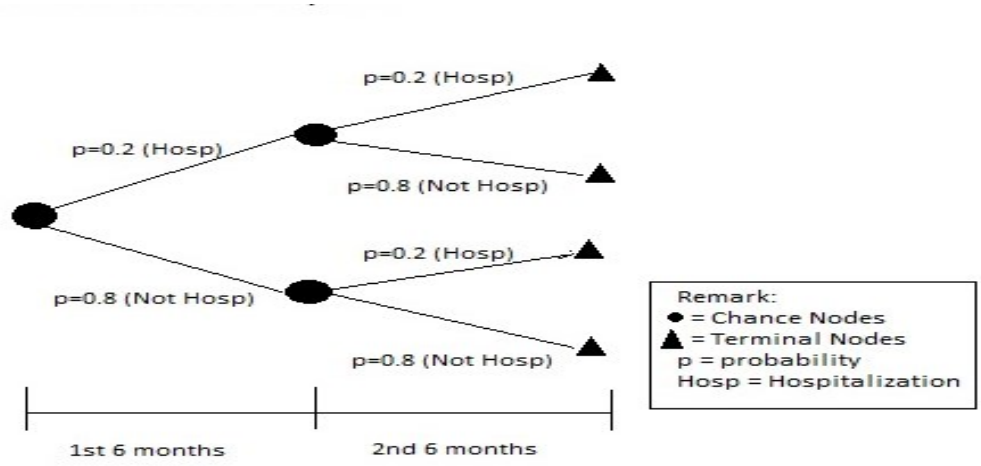
No additional device/system related complications or sensor failures occurred during the remainder of the Randomized Access period (beyond the 6-month primary endpoint period) or during the Open Access period of the trial. Hence, there were 8 device system related complications and no sensor failures over an experience of 1167 patient-years (mean follow-up period of 26 months with longest follow-up of 3.6 years).

Number of patients (in Norway) the proposed technology may be appropriate for?

As of April 01, 2015, the population of Norway is 5,176,998.[8] The findings from the Hillingdon HF study in the United Kingdom showed that the incidence of definitive HF was 9.3/1000 per year with a mean age of the population with definitive heart failure being 77 years of age.[9]

Doctors usually classify patients' HF according to the severity of their symptoms. The New York Heart Association (NYHA) Functional Classification is commonly used. It places patients in one of four categories based on how much they are limited during physical activity.[10] The initial state distribution of NYHA Class III patient is about 23%.[11] The probability of NYHA Class III patients that requires hospitalization in a six-month period is 0.2.[11] The following diagram shows the probability of NYHA Class III patients who may require hospitalization in a 12-month period.

Diagram 1 – The probability of NYHA Class III Patients who require hospitalization in a 12-month period



The probability of NYHA Class III patients who may be hospitalised once in a 12-month period is 0.2*0.2 + 0.2*0.8 + 0.8*0.2 = 0.36.

By extension the estimated number of patients which may benefit from heart failure therapy guided by continuous pulmonary artery pressure monitoring are approximately 5,176,998*0.0093*0.23*0.36 = 3,986.50.

In summary it is believed that close to 4,000 patients per annum could benefit from the technology (NYHA class III HF patients with at least one previous heart failure hospitalisation)

Use of health care resources (equipment, personnel etc)

Elevations in PA pressures are observable several days prior to worsening signs and symptoms that lead to HF hospitalizations. Medication and/or other therapy changes made in response to elevated PA pressures allows for earlier intervention by physicians to prevent these events and improve clinical outcomes for their patients. An elevation of PA pressures should be considered a volume overloaded status. Response to these signs are dependent on the doctors clinical opinion but in most cases doctors start with intensification of diuretic therapy to reduce the elevated PA pressures followed by vasodilator therapy, primarily using long-acting nitro-glycerine therapy, in those patients where PA pressures continue to remain elevated in order to achieve successful volume depletion. Most will pursue a similar strategy as an episode of acute heart failure but of course the therapy can be less aggressive as there is more time to stabilise the patient prior to the volume overload triggering an episode of full decompensation.

NICE have published a care pathway for the treatment of chronic heart failure and the CardioMEMS Heart failure system clearly fits within the “treatment and monitoring” section[4]. Indeed, pulmonary artery pressure monitors are referred to in this section and there is a NICE interventional procedure guidance (463) on “insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure”[6].

The need to revise the existing national professional guidelines

Norwegian guidelines for heart failure treatment are based on the European Society of Cardiology guidelines.

Specialist centres, where this technology will be best implemented, develop their own care pathways based on these guidelines. Pulmonary artery pressure guided treatment using CardioMEMS can be easily integrated into these care pathways because the system does not replace guideline recommended therapy but offers an opportunity to optimise therapy based on real time monitoring of a disease relevant physiological signal.[12]

13. Please enter references to documentation about the method's efficiency and safety (eg. Former HTAs, Up to 10 references may be given. Do not send attachments at this stage of the process)

1. Abraham, W. T. et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. The Lancet 377, 658-666, doi:10.1016/s0140-6736(11)60101-3 (2011).
2. Abraham, W. T. et al. Safety and accuracy of a wireless pulmonary artery pressure monitoring system in patients with heart failure. American heart journal 161, 558-566, doi:10.1016/j.ahj.2010.10.041 (2011).
3. Abraham, W. T. et al. Trials of implantable monitoring devices in heart failure: which design is optimal? Nature reviews. Cardiology 11, 576-585, doi:10.1038/nrcardio.2014.114 (2014).
4. Adamson, P. B. et al. CHAMPION trial rationale and design: the long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. J Card Fail 17, 3-10, doi:10.1016/j.cardfail.2010.08.002 (2011).
5. Adamson, P. B. et al. Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. Circulation. Heart failure 7, 935-944, doi:10.1161/circheartfailure.113.001229 (2014).
6. Benza, R. L. et al. Pulmonary hypertension related to left heart disease: Insight from a wireless implantable hemodynamic monitor. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, doi:10.1016/j.healun.2014.04.014 (2014).
7. Castro, P. F. et al. A wireless pressure sensor for monitoring pulmonary artery pressure in advanced heart failure: initial experience. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation 26, 85-88, doi:10.1016/j.healun.2006.10.006 (2007).
8. Krahnke, J. S. et al. Heart Failure and respiratory hospitalizations are reduced in heart failure subjects with chronic obstructive pulmonary disease using an implantable pulmonary artery pressure monitoring device. J Card Fail, doi:10.1016/j.cardfail.2014.12.008 (2014).
9. Ritzema, J. et al. Physician-directed patient self-management of left atrial pressure in advanced chronic heart failure. Circulation 121, 1086-1095, doi:10.1161/circulationaha.108.800490 (2010).

14. Please provide the name of the manufacturers / suppliers regarding the technology if possible

St Jude Medical Inc.
One St Jude Medical Drive
St Paul, Minnesota 55117
USA

15. Status for Marked authorization (MA) or CE-marking: (At what time is MA expected? Is there a planned time for marketing the proposed technology?)

The CardioMEMS HF System first obtained CE marking in 2011 and the current CE marking was completed with BSI on 1st May 2014.

The CardioMEMS HF System received US FDA approval on May 28, 2014.

16. Additional relevant information, up to 300 words

In order to put the treatment effect size of the CardioMEMS HF System into an appropriate context, the treatment effect observed in CHAMPION can be compared to the treatment effect observed in other pivotal HF drug trials for ACCF/AHA and ESC guideline directed medical therapies ACE inhibitors, angiotensin receptor blockers, beta blockers, aldosterone antagonists, and digoxin.

The CardioMEMS HF System had an equivalent or greater treatment effect than HF drug therapy trials for HF hospitalization rates, mortality, deaths and HF hospitalization rates, and total deaths and all-cause hospitalization rates. These data demonstrate the substantial clinical improvement over standard of care physicians could provide to HF patients by using the CardioMEMS HF System. It is important to note that patients in the CHAMPION trial were required to have been treated with all appropriate drug and device treatments for heart failure at optimal or best-tolerated stable doses prior to enrolment in accordance with ACCF/AHA guidelines. Therefore, the treatment effect observed in the CHAMPION trial using the CardioMEMS HF System could be considered as incremental to the benefit associated with the current guideline recommended standard of care.

References

1. Dickstein, K., et al., *ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM).* Eur Heart J, 2008. **29**(19): p. 2388-442.
2. McMurray, J.J., et al., *ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC.* Eur Heart J, 2012. **33**(14): p. 1787-847.
3. Abraham, W.T., et al., *Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial.* The Lancet, 2011. **377**(9766): p. 658-666.
4. (NICE), N.I.f.H.a.C.E., *Chronic heart failure treatment and monitoring pathway*, in *Chronic heart failure pathway*. 2014, UK.
5. Stewart, S., et al., *More 'malignant' than cancer? Five-year survival following a first admission for heart failure.* Eur J Heart Fail, 2001. **3**(3): p. 315-22.
6. (NICE), N.I.f.H.a.C.E., *Insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure*, in *Nice interventional procedure guidance*. 2013.

7. Tuppin, P., et al., *First hospitalization for heart failure in France in 2009: patient characteristics and 30-day follow-up.* Arch Cardiovasc Dis, 2013. **106**(11): p. 570-85.

8. Statistics Norway, https://www.ssb.no/en

9. K. Guha and T. *McDonagh, Heart Failure Epidemology: European Perspective.* Curr Cardiol Rev. 2013 May; **9**(2): 123–127.

10. Classes of Heart Failure. American Heart Association. http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp

11. Patricia A. Cowper, PhD, et al., *Economic Effects of Beta-Blocker Therapy in Patients with Heart Failure.* Am J Med. 2004; **116**: 104-111.

12. Tove Rosstad, et al., *Development of a patient-centred care pathway across healthcare providers: a qualitative study.* BMC Health Services Research 2013, **13**:121.